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| 09/756,092      | 01/08/2001  | Michael J. Cima      | 10436-0009-999      | 5650             |

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EXAMINER

BAKER, MAURIE GARCIA

ART UNIT PAPER NUMBER

1639

DATE MAILED: 10/23/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/756,092

Applicant(s)

Cima et al

Examiner

Maurie G. Baker, Ph.D.

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jul 10, 2003
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 170-179 is/are pending in the application.
- 4a) Of the above, claim(s) 170, 172-174, and 176 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 171, 175, and 177-179 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 22 6) ☐ Other:

### DETAILED ACTION

1. The Response filed July 10, 2003 (Paper No. 21) is acknowledged. No claims were cancelled, amended or added. Therefore, claims 170-179 are currently pending.
2. As stated in the previous action, since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 174 and claims 178-179 (in part) are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.
3. Applicant's election without traverse with respect to claims 170-173, 175-177 and 178-179 (in part) is acknowledged. Note that the previous election requirement is still in effect, in as much as it reads on the new claims 170-179. Applicant has elected Species 2: method of identifying (crystalline) salts; claims 171, 175 & 177-179 (in part).
4. As applicant's elected species was found in the art, claims 170, 172, 173, 176 & 177-179 (in part) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected *species*, there being no allowable generic or linking claim. Note that the search has not been extended to all non-elected species. Also please note MPEP § 803.02 with respect to species elections.

***Status of Rejections & Response to Arguments***

5. The previous claim rejections are withdrawn in view of applicant's amendments (cancellation of claims and addition of new claims). As the below rejections are necessitated by applicant's amendments, this action is made final. Also, applicant's arguments from the Response filed April 4, 2003 have been considered but are moot in view of the new ground(s) of rejection set forth in this action.

***New Rejections -- Necessitated by Amendment  
Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 171, 175 and 179 (in part) are rejected under 35 U.S.C. 103(a) as being unpatentable over Morris et al (Int. J. of Pharmaceutics, 1994) in view of Hol et al (US 6,267,935; of record) and Stylli et al (US 5,985,214; of record).

Morris et al teach a method to identify an optimal salt form for BMS-180431 (see Abstract). BMS-180431 is a HMG-CoA reductase inhibitor, reading on the claimed "small molecule pharmaceutical" (see Abstract and page 211). Physiochemical properties of seven salts were studied using a "multi-tier approach" (see Abstract and page 210). At least two of the samples of the reference comprise a salt and one of the at least two samples is different from another. See Figures 2, 3 and 4 and Table 1 of the reference (and associated text). This reads on the instant steps (b) and (c) of claim 171 and the instant steps (b) and (c) of claim 175. This also reads on the differences between the samples set forth in instant claim 175. Once the optimal salts were determined, these compounds were further screened versus excipients and for stability. See Section 2 on pages 210-211 and Section 3.8 on page 213. This further reads on the instant step (c) of claim 175 with respect to "filtering means" and "grouping". Also, as samples were analyzed by HPLC with UV absorbance detection (see Section 3.9 on pages 213-214), this reads on "analyzing the processed samples using spectroscopy" of instant claim 171.

Morris et al lacks the specific teaching of preparing an array of at least 24 samples and the specific sample size as claimed.

However, preparing arrays of 24 or more samples and using samples of such size was well established in the art at the time of filing. For example, Hol et al teach a method useful in the crystallization of proteins and other molecules using plates with a plurality of reservoirs and four sets of 48 different crystallization solutions (see Abstract,

Figure 1 and Tables 1-4). The process of Hol et al permits “a large number of crystallization conditions to be easily and simultaneously tested in order to identify conditions under which a target molecule...can be crystallized” (column 3, lines 3-11). Hol et al teach testing at least 24 conditions (see plate of Figure 1, also the four sets of 48 different crystallization solutions), which differ in their components and/or temperature, for example (see Tables 1-4 and column 9, line 54 through column 10, line 64). The reference also discloses that other parameters can be varied, as needed for best crystal formation (see column 11, lines 21-33). The samples are examined for crystal formation via visual inspection or microscopy (column 11, lines 8-20). The reference discloses crystallization of five different proteins (see Examples 1-5) where samples are processed and crystals are detected in each. The reference discloses using amounts of protein in the 20-60 microgram range in the specific crystallization examples (Examples 1-5).

Moreover, the optimization of such variables was well established in the art of high-throughput testing, see for example, Stylli et al in general and specifically columns 43 – 44 and 48 for teachings of numbers of samples tested, number per day and amounts.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the method of Morris et al for any number of samples and any amount of active component. One of ordinary skill would have been motivated to do so due in order to test a large number of samples and also optimize the method for the desired particular active ingredient as such was well established in the art (as demonstrated by Hol et al and Stylli et al).

9. Claims 171, 175 and 177 & 178 (in part) are rejected under 35 U.S.C. 103(a) as being unpatentable over Morris et al (Int. J. of Pharmaceutics, 1994) in view of Hol et al (US 6,267,935; of record) and Stylli et al (US 5,985,214; of record) as set forth above, and further in view of Findlay et al (J. Pharm. Biomed. Analysis, 1998; on PTO-1449).

The teachings of Morris, Hol and Stylli are set forth supra.

The references lack the teaching of specifically using Raman spectroscopy.

However, the use of Raman spectroscopy for such analyses was well established in the art at the time of filing. For example, Findlay et al teach the use of FT-Raman to differentiate between crystal forms of a drug substance (see Abstract). The reference also teaches the advantages of using such a technique and the set-up required.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the method of Morris et al for any number of samples and any amount of active component (as demonstrated by Hol et al and Stylli et al) and to further use Raman spectroscopy for analysis as demonstrated by Findlay et al. One of ordinary skill would have been motivated to do so due in order to test a large number of samples and also optimize the method for the desired particular active ingredient as such was well established in the art. One would have been specifically motivated to use Raman spectroscopy to enhance characterization and obtain qualitative and semi-quantitative information (see Findlay et al, Conclusions, pages 929-930).

#### ***Status of Claims/Conclusion***

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

13. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to



the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.  
October 20, 2003



**MAURIE GARCIA BAKER PH.D**  
**PRIMARY EXAMINER**